

unless the context clearly dictates otherwise. Thus, for example, reference to “an analyte” includes a plurality of such analytes and reference to “the channel” includes reference to one or more channels and so forth.

**[0030]** Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood to one of ordinary skill in the art to which this disclosure belongs. Although methods and materials similar or equivalent to those described herein can be used in the practice of the disclosed methods and compositions, the exemplary methods, devices and materials are described herein.

**[0031]** The publications described herein are provided solely for their disclosure prior to the filing date of the present application. Nothing herein is to be construed as an admission that the inventors are not entitled to antedate such disclosure.

**[0032]** Small regulatory RNA molecules, such as microRNAs (miRNAs) and short interfering RNAs (siRNAs), play an important role in regulation of gene expression in various organisms by binding to the target mRNAs through sequence complementation (Liu et al., *Proc. Natl. Acad. Sci.*, 2004, 101:9740-9744). miRNAs are a class of small (~18-24 nt, nucleotide) non-protein coding RNA molecules cleaved from ~70 nt-long hairpin precursor (pre-miRNA) [Science 2001, 294:853-858], which is enzymatically processed from the long primary transcript (pri-miRNA) (Jinek et al., *Nature*, 2009, 457:405-412). The regulatory role of miRNAs is conducted by incorporating into an active RNA-induced silencing complex (RISC) and resulting in translational repression or degradation of specific target mRNAs (Bartel et al., *Cell*, 2004, 116:281-297; *Genes Dev* 2006, 20:515-524). It's estimated that hundreds of miRNAs are encoded in the human genome, dozens of which have now been shown to regulate a diverse variety of cellular processes, both in normal physiology and in disease. (Lu et al., *Nature*, 2005, 435:834-838). Expression profiles of miRNAs are thought to contain potential diagnostic and prognostic information for various types of tumors (Calin et al., *Nat Rev Cancer*, 2006, 6:857-866; Garzon et al., *Trends Mol Med* 2006, 12:580-587).

**[0033]** Challenges exist for the detection of miRNAs with high specificity, sensitivity and accuracy due to their intrinsic characteristics, such as the extremely small size, highly similar sequences (between both the miRNA family members and the mature and precursor miRNAs, pri-miRNAs and pre-miRNAs), small mass fraction (ca. 0.01%) in the total RNA sample and the largely varied relative expression levels (Bartel, *Cell*, 2004, 116:281). Different approaches have been developed to detect miRNAs, such as Northern blot analysis with radiolabeled probes (Valoczi et al., *Nucleic Acids Res*, 32: e175, 2004), microarray-based (Thomson et al., *Nat Methods* 1:47-53, 2004), and PCR-based methods (Griffiths-Jones et al., *Nucleic Acids Res* 33:e179, 2005), in situ hybridization (Klosterman et al., *Nat Methods* 3:27-29, 2006), and high-throughput sequencing (Schulte et al., *Nucleic Acids Res* 38:5919-5928, 2010). Conventionally, miRNA detections are based on the off-line purified total RNA samples or enriched small RNA fractions with the consumption of large sample/reagent volumes. With the separated procedures of total RNA purification and subsequent miRNA detection, these methods are time- and reagent-consuming, non-continuous and difficult to automate, which makes them not ideal for future miRNA diagnostics.

**[0034]** By virtue of their capabilities of flexible combination and dense integration of functional units, reduction in

instrument size and sample/reagent consumption, and enhancement of sensitivity, microfluidic devices have emerged as promising technologies for Lab-on-a-chip genetic analysis. To date, a number of microfluidic systems have been developed to perform nucleic acid purification and detection in stand-alone or integrated format. Among these, magnetic droplet-based microfluidic platforms present special features such as simplicity of fabrication, easiness of operation and flexibility of application. Because the magnetic interaction is unaffected by surface charges, pH, ionic strength or temperature, it is compatible with a wide range of substrate materials and (bio) chemical processes. These valveless/pumpless and interface-free microdevices are low-cost, portable and compatible with point-of-care applications. When using silica superparamagnetic particles (SMPs) for genetic analysis the SMP-droplet itself becomes a droplet actuator and nucleic acid solid-phase extractor, even a real-time thermocycler. Despite the unique properties mentioned above, existing SMP-based microsystems face big challenges when it comes to the parallel manipulation of multiple magnetic droplets, or the processing of complex analytes such as miRNAs, which require additional SMP-binding step to remove large DNA/RNA molecules in samples.

**[0035]** The disclosure provides a multi-well/microchannel-array (M2) chip platform for magnetic droplet-based, parallel miRNA purification and reaction/detection. Furthermore, the disclosure provides a rapid and cost-effective prototyping technique based upon an optical adhesive for one-step replication of PDMS chip.

**[0036]** The disclosure demonstrates that methods, devices and manufacturing methods through a simple and convenient manipulation of multiple SMP droplets on the M2 chip by using a syringe pump-based handling stage. For example, the disclosure demonstrates the selective binding and extraction of miRNAs from 63 nt RNA molecules, and results of the characterization of the M2 chip-based miRNA purification. Furthermore, the disclosure demonstrates the integration of solid-phase extraction (SPE) and RT reaction of has-mir-191 from lysates of two cell lines. From these results, the development of the presented M2 chip platform for high throughput and sample-to-answer analysis and diagnostics of miRNAs from biological samples is clearly demonstrated.

**[0037]** Temperature control elements can be optionally present to control evaporation or condensation of fluid flowing through the fluid flow channel. In one aspect, temperature control element comprises a cooling element that reduces the evaporative capacity of a fluid flowing through the system.

**[0038]** Referring now to FIG. 1D a general diagram of a device and system of the disclosure is provided. Device **10** comprises a substrate **20** and a plurality of wells **30** and a trap well **35** fluidly connected by channels **40**. The example depicted in FIG. 1D shows four channels; however, there need only be one channel and the upper limit of channels is only limited by the size of the substrate **20**. Accordingly, the number of channels of the device can comprise from 1 to 10 or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 etc.). Furthermore, FIG. 1D shows 7 wells **30** and a trap well **35**. The device and system are not limited by the number of wells so long as there are at least 2. Accordingly, the number of wells may be from 1 to 30 or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 . . . etc.). The channels and well contain different fluid materials (**60** and **70**). Typically the fluid materials **60** and **70** are immiscible such as an aqueous fluid and an oil fluid. The wells **30** confine the aqueous droplets **60** with different components and the